

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

RECEIVED

To:

WEBSTER, Thomas D. ✓
ELI LILLY AND COMPANY
Lilly Corporate Center
Indianapolis, Indiana 46285
ETATS-UNIS D'AMERIQUE

JAN 04 2002 PCT

ELI LILLY & COMPANY
PATENT NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing (day/month/year)	14.12.2001
-------------------------------------	------------

Applicant's or agent's file reference
X-13268

IMPORTANT NOTIFICATION

International application No.
PCT/US00/20806

International filing date (day/month/year)
31/08/2000

Priority date (day/month/year)
10/09/1999

Applicant
ELI LILLY AND COMPANY

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.


4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/


 European Patent Office
 D-80298 Munich
 Tel. +49 89 2399 - 0 Tx. 523656 epmu d
 Fax: +49 89 2399 - 4465

Authorized officer

Hingel, W

Tel. +49 89 2399-8717



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference X-13268	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/20806	International filing date (day/month/year) 31/08/2000	Priority date (day/month/year) 10/09/1999
International Patent Classification (IPC) or national classification and IPC C12N15/12		
Applicant ELI LILLY AND COMPANY		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 6 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I Basis of the report
- II Priority
- III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

Date of submission of the demand 02/03/2001	Date of completion of this report 14.12.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Pilat, D  Telephone No. +49 89 2399 8668

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/20806

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-35 as originally filed

Claims, No.:

1-13 as originally filed

Drawings, sheets:

1/1 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
 - the language of publication of the international application (under Rule 48.3(b)).
 - the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- contained in the international application in written form.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority in written form.
 - furnished subsequently to this Authority in computer readable form.
 - The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/20806

- the drawings, sheets:
5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):
(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)
6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims
	No: Claims 1-4
Inventive step (IS)	Yes: Claims
	No: Claims 5-13
Industrial applicability (IA)	Yes: Claims 1-13
	No: Claims

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/20806

1. Reference is made to the following documents:

- D1: WO 98 30694 A (HUMAN GENOME SCIENCES INC ;FENG PING (US); NI JIAN (US); EBNER REI) 16 July 1998 (1998-07-16)
- D2: YU K-Y ET AL.: 'A newly identified member of tumor necrosis factor receptor superfamily (TR6) suppresses LIGHT-mediated apoptosis' JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 274, no. 20, 14 May 1999 (1999-05-14), pages 13733-13736, XP002161940
- D3: WO 00 58465 A (BECKER GERALD WAYNE ;COHEN FREDRIC JAY (US); GONZALEZ DEWHITT PATR) 5 October 2000 (2000-10-05)

Ad Section V :Reasoned statement under Rule 66.2(a)(ii); citations and explanations supporting such statement

2. Novelty (Article 33 (2) PCT)

- 2.1 D1 describes pharmaceutical compositions containing TNFR proteins (e.g. TNFR-6 α and -6 β proteins), wherein said carrier may be a Ringer's solution. This solutions contains CaCl_2 at an end concentration of approximately 0,3 mg/ ml and MgCl_2 (see p.45 line 35 to p.47 line 2). It is further emphasized that claims 1,4 are referring to a resistance to proteolysis in general terms, i.e. that any "FLINT" "analog" which is resistant **to at least one** protease is encompassed by this claim language. Thus, claims 1-4 lacks novelty.
- 2.2 D2 describes TR-6(His) which was passed through a Ni-column. Thus, claims 1,2,4 lack novelty.

3. Inventive step (Article 33 (3) PCT)

- 3.1 D2 describes a TR-6 tagged protein. It is however well known that Ni-NTA may be replaced by any other divalent cations chelate (e.g. Zn^{2+}). Thus, dependent claims 3 lacks an inventive step.
- 3.2 D1 states that TNFR 6 α and 6 β receptor proteins may be altered to enhance or increase stability, solubility etc.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/20806

In order to reduce proteolytical degradation of a protein of interest, the skilled person would have modified its sequence to such an extent that said problem is reduced or even abolished by mutants screening. In the absence of any surprising effect associated with "FLINT" analogs having R218Q, this specific solution seems to be one out of a myriad the skilled person would have selected without inventive activity.

Insofar as the mutated protein and the divalent cation solves different problems and neither of them are inventive, the juxtaposition claimed in claim 5 lacks an inventive step. The same applies to pharmaceutical compositions as claimed in 6-8 which specifies only the total cation concentration.

- 3.3 Claim 9 relates to a process of reducing aggregation of a protease-resistant "FLINT" analog molecule, comprising removing divalent cation.

"Salting out" proteins is a well known technique, wherein addition of specific metal cations such as Zn^{2+} , Cd^{2+} and Ba^{2+} or of compounds with bulky anions can precipitate proteins at appropriate pH values. The addition of salts represents therefore a perturbation that can cause certain proteins to precipitate, which corresponds to an extreme aggregation phenomenon.

In order to avoid precipitation or aggregation of proteins in solution, it is obvious according to general knowledge, as one potential solution to remove salt, by complexation e.g. with EDTA, or to reduce its concentration by dilution (e.g. dialysis). In view of this rationale, claim 9 seems trivial.

The same conclusion applies to dependent claims 10,11 as well as to claims 12 and 13 which are applying this teaching.

- 3.4 It is further underlined that D1 discloses Zn^{2+} as an antagonist of TNFR 6 α and 6 β receptor proteins. Based on D1 no inventive activity can be either acknowledged for adding Zn^{2+} to a cell in order to limit apoptosis induced by Fas ligand (see p.39 line 36 to p.40 line 12, p.42 line 13). Thus, in any event claims 1-4 lacks an inventive step.

Ad Section VI : Certain documents

- 4) **Certain published documents (Rule 70.10)**

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/20806

Certain published documents (Rule 70.10)

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO-00 58465	5/10/2000	20/3/2000	30/3/1999

Ad Section VIII : Certain observations on the international application.

5. Clarity (Article 6 PCT)

Claim 1 lacks clarity, because the terms "FLINT" and "analog" used has not an accepted meaning in the art. As such they render the scope of protection unclear. The same objections applies to all the claims using such a term.

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
15 March 2001 (15.03.2001)

PCT

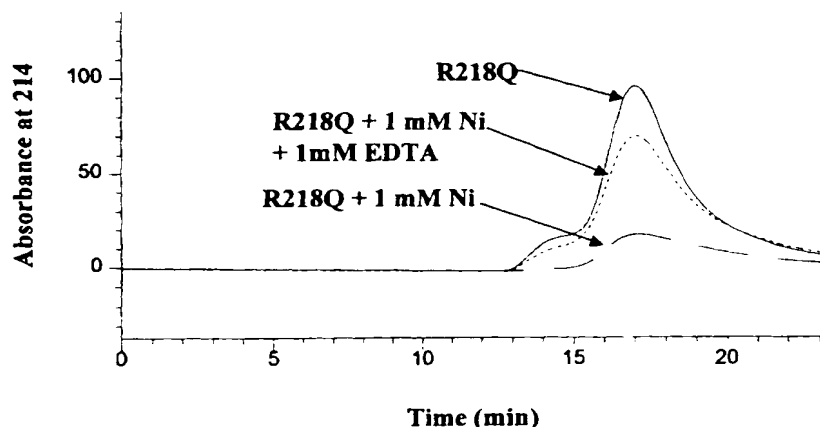
(10) International Publication Number
WO 01/18202 A2

- (51) International Patent Classification: C12N 15/12, C07K 14/705, 1/30, A61K 38/17, 33/30
- (21) International Application Number: PCT/US00/20806
- (22) International Filing Date: 31 August 2000 (31.08.2000)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/153,433 10 September 1999 (10.09.1999) US
- (71) Applicant (for all designated States except US): ELI LILLY AND COMPANY [US/US]; Lilly Corporate Center, Indianapolis, IN 46285 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): ATKINSON, Paul, Robert [US/US]; 4514 Lakeside Drive, Indianapolis, IN 46234 (US). TIAN, Yu [CN/US]; 13695 Flintridge Pass, Carmel, IN 46033 (US). WITCHER, Derrick, Ryan [US/US]; 10898 Parrot Court, Fishers, IN 46038 (US).
- (74) Agents: WEBSTER, Thomas, D. et al.; Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:
Without international search report and to be republished upon receipt of that report.

[Continued on next page]

(54) Title: FLINT ANALOG COMPOUNDS AND FORMULATIONS THEREOF

Interaction of R218Q His-tagged FLINT Analog with Ni²⁺



(57) Abstract: The present invention provides novel compounds, which comprise a protease-resistant FLINT analog complexed with a divalent metal cation, pharmaceutical formulations thereof, and methods of using such compounds for treating or preventing diseases related to the FasL/Fas interaction.

WO 01/18202 A2



For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
15 March 2001 (15.03.2001)

PCT

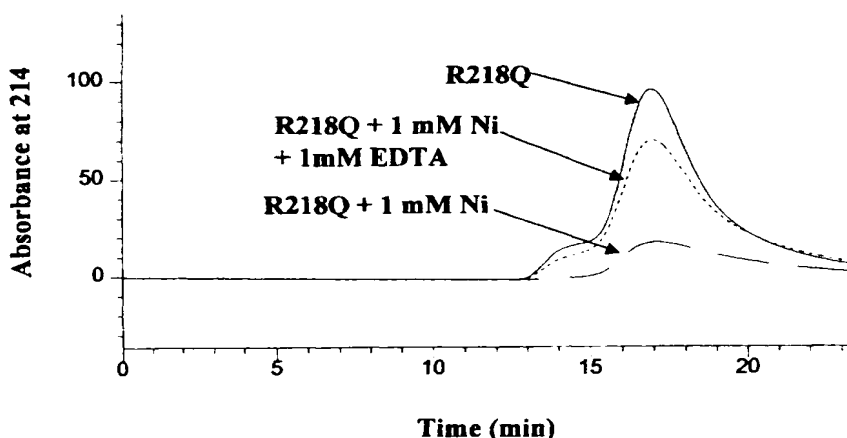
(10) International Publication Number
WO 01/18202 A3

- (51) International Patent Classification⁷: C12N 15/12, C07K 14/705, 1/30, A61K 38/17, 33/30
- (21) International Application Number: PCT/US00/20806
- (22) International Filing Date: 31 August 2000 (31.08.2000)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 60/153,433 10 September 1999 (10.09.1999) US
- (71) Applicant (for all designated States except US): ELI LILLY AND COMPANY [US/US]; Lilly Corporate Center, Indianapolis, IN 46285 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): ATKINSON, Paul, Robert [US/US]; 4514 Lakeridge Drive, Indianapolis, IN 46234 (US). TIAN, Yu [CN/US]; 13695 Flintridge Pass, Carmel, IN 46033 (US). WITCHER, Derrick, Ryan [US/US]; 10898 Parrot Court, Fishers, IN 46038 (US).
- (74) Agents: WEBSTER, Thomas, D. et al.; Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published: — with international search report
- (88) Date of publication of the international search report: 7 September 2001

[Continued on next page]

(54) Title: FLINT ANALOG COMPOUNDS AND FORMULATIONS THEREOF

Interaction of R218Q His-tagged FLINT Analog with Ni²⁺



(57) Abstract: The present invention provides compounds, which comprise a protease-resistant FLINT analog complexed with a divalent metal cation, pharmaceutical formulations thereof, and methods of using such compounds for treating or preventing diseases related to the FasL/Fas interaction.



A3



For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

Inte Application No

PCT/US 00/20806

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/705 C07K1/30 A61K38/17 A61K33/30

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 30694 A (HUMAN GENOME SCIENCES INC ;FENG PING (US); NI JIAN (US); EBNER REI) 16 July 1998 (1998-07-16) page 42, line 13 example 1 ---	9-11
A	YU K-Y ET AL.: "A newly identified member of tumor necrosis factor receptor superfamily (TR6) suppresses LIGHT-mediated apoptosis" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 274, no. 20, 14 May 1999 (1999-05-14), pages 13733-13736, XP002161940 abstract page 13734, left-hand column, line 21-35 --- -/--	1,9

Further documents are listed in the continuation of box C. Patent family members are listed in annex

* Special categories of cited documents

A document defining the general state of the art which is not considered to be of particular relevance *E* earlier document but published on or after the international filing date *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) *O* document referring to an oral disclosure, use, exhibition or other means *P* document published prior to the international filing date but later than the priority date claimed	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention *X* document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone *Y* document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. *&* document member of the same patent family
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Date of the actual completion of the international search	Date of mailing of the international search report
2 March 2001	22/03/2001

Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel (+31-70) 340-2040. Tx. 31 651 epo nl. Fax. (+31-70) 340-3016	Authorized officer van de Kamp, M
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/20806

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
E	WO 00 58465 A (BECKER GERALD WAYNE ; COHEN FREDRIC JAY (US); GONZALEZ DEWHITT PATR) 5 October 2000 (2000-10-05) example 4 -----	1, 4-6, 9-13

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/20806

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9830694	A	16-07-1998	AU 729062 B	25-01-2001
			AU 5815798 A	03-08-1998
			AU 6238698 A	03-08-1998
			BR 9806954 A	21-03-2000
			CN 1247567 T	15-03-2000
			EP 1007659 A	14-06-2000
			EP 0990031 A	05-04-2000
			WO 9830693 A	16-07-1998
WO 0058465	A	05-10-2000	AU 3739400 A	16-10-2000
			AU 3739500 A	16-10-2000
			WO 0058466 A	05-10-2000

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference X-13268	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 00/20806	International filing date (day/month/year) 31/08/2000	(Earliest) Priority Date (day/month/year) 10/09/1999
Applicant ELI LILLY AND COMPANY		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

contained in the international application in written form.

filed together with the international application in computer readable form.

furnished subsequently to this Authority in written form.

furnished subsequently to this Authority in computer readable form.

the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. **Certain claims were found unsearchable** (See Box I).

3. **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

as suggested by the applicant.

because the applicant failed to suggest a figure.

because this figure better characterizes the invention.

None of the figures.

INTERNATIONAL SEARCH REPORT

national application No.

PCT/US 00/20806

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

On line 1: delete "novel" before "compounds"

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/20806

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/705 C07K1/30 A61K38/17 A61K33/30

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	WO 98 30694 A (HUMAN GENOME SCIENCES INC ; FENG PING (US); NI JIAN (US); EBNER REI) 16 July 1998 (1998-07-16) page 42, line 13 example 1	9-11
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Further documents are listed in the continuation of box C

Patent family members are listed in annex

Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *Z* document member of the same patent family

Date of the actual completion of the international search

2 March 2001

Date of mailing of the international search report

22/03/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
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Fax (+31-70) 340 3016

Authorized officer

van de Kamp, M

INTERNATIONAL SEARCH REPORT

International Application No
 /US 00/20806

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E ✓	WO 00 58465 A (BECKER GERALD WAYNE ;COHEN FREDRIC JAY (US); GONZALEZ DEWHITT PATR) 5 October 2000 (2000-10-05) example 4 -----	1, 4-6, 9-13

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/20806

Patent document cited in search report	A	Publication date		Patent family member(s)	Publication date
WO 9830694	A	16-07-1998		AU 729062 B	25-01-2001
				AU 5815798 A	03-08-1998
				AU 6238698 A	03-08-1998
				BR 9806954 A	21-03-2000
				CN 1247567 T	15-03-2000
				EP 1007659 A	14-06-2000
				EP 0990031 A	05-04-2000
				WO 9830693 A	16-07-1998
WO 0058465	A	05-10-2000		AU 3739400 A	16-10-2000
				AU 3739500 A	16-10-2000
				WO 0058466 A	05-10-2000

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year) 08 January 2002 (08.01.02)	Applicant's or agent's file reference X-13268
International application No. PCT/US00/20806	Priority date (day/month/year) 10 September 1999 (10.09.99)
International filing date (day/month/year) 31 August 2000 (31.08.00)	
Applicant ATKINSON, Paul, Robert et al	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

 02 March 2001 (02.03.01)

in a notice effecting later election filed with the International Bureau on:

2. The election was
 was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer ALI SOLEIMAN
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38